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ORIGINAL ARTICLE

Percutaneous cementoplasty in multiple myeloma: a valuable adjunct for pain control and ambulation maintenance

Nhu Nam Tran Thang · German Abdo · Jean-Baptiste Martin · Yodit Seium-Neberay · Hasan Yilmaz · Marie-Christine Verbist · Daniel Rufenacht · Andre-Pascal Sappino · Pierre-Yves Dietrich

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Abstract
Goals of work Bone pain and functional impairment are major concerns for multiple myeloma (MM) patients. The goal of this study was to better define the role of percutaneous cementoplasty (PC) in improving their quality of life.
Materials and methods This retrospective analysis included 28 consecutive heavily pretreated MM patients managed at our institution between 1996 and 2002. They underwent a total of 34 PC procedures for the treatment of 117 vertebrae and 2 iliac sites and were evaluated at 1 month.
Main results Significant pain reduction of >50% was obtained after 83% of the procedures, with a mean visual analogous score decreasing from 7.48/10 to 2.1/10 ($p<0.001$). It resulted in a complete interruption of opiate analgesic consumption after 59.3% of the procedures, with a mean decrease of 70.4% in the opiate dose. Functional impairment was evaluated with the Eastern Cooperative Oncology Group (ECOG) performance status scale, with mean scores improving from 1.9 to 0.86 after the procedures ($p=0.001$). There was no major complication.
Conclusion PC is a safe, feasible, and efficient approach for the treatment of bone pain and disability in MM patients.

Keywords Bone metastasis · Pain · Vertebral compression fracture · Vertebroplasty

N. N. Tran Thang · Y. Seium-Neberay · M.-C. Verbist · A.-P. Sappino · P.-Y. Dietrich (✉)
Division of Oncology, Geneva University Hospital,
21 rue Micheli-du-Crest,
1211 Geneva 14, Switzerland
e-mail: Pierre-Yves.Dietrich@hcuge.ch

G. Abdo · J.-B. Martin · H. Yilmaz · D. Rufenacht
Department of Radiology, Geneva University Hospital,
21 rue Micheli-du-Crest,
1211 Geneva 14, Switzerland

Introduction

Although currently available therapies have significantly prolonged disease-free and overall survival, multiple myeloma (MM) remains an incurable disorder, characterized by frequent relapses and ultimate resistance to antitumoral agents. Hence, skeletal morbidity contributes persistently to alter the quality of life of many myeloma patients, despite the recognized impact of localized or even extended radiation therapy, biphosphonates [16], and surgical interventions [9, 30].

Initially used for the treatment of benign conditions such as hemangioma and osteoporotic fractures [4, 10, 12], percutaneous cementoplasty (PC) has since been shown to provide significant pain relief in bone lesions resulting from diverse metastatic neoplasia [11, 14, 17, 21]. Indications for PC and patient selection have been extended [3, 5, 15, 18, 23, 28] to be applied to flat vertebrae and also to extravertebral sites. Studies with limited numbers of patients have also documented the beneficial effects of PC for management of vertebral compression fractures related to MM [2, 6, 24].

This study describes the effects of PC in a retrospective series of 28 consecutive MM patients treated at our institution between 1996 and 2002, who suffered from refractory pain related to bone infiltration by the disease, with or without associated bone fractures.

Materials and methods

Patients

We reviewed nonselected MM patients subjected to PC between 1996 and 2002 at our institution. MM diagnosis was made on the basis of the presence of a monoclonal protein, bone manifestations, and on bone marrow plasma cell infiltration [8]. Staging was established according to Durie–Salmon criteria [7]. Patients' characteristics (n=28) are summarized in Table 1. Most of the patients were heavily pretreated, with bone pain refractory to conventional therapies. Indications for PC were systematically debated preoperatively by a multidisciplinary team, including a neurosurgeon, an orthopedic surgeon, a medical oncologist, a radio-oncologist, an anesthesiologist, and interventional radiologists. Decision to perform PC was made when spontaneous or palpation elicited pain correlated with radiological evidence of tumoral infiltration, using computed tomography (CT) scan and/or magnetic resonance imaging. Adjacent levels, which are known to be at increased risk for secondary fractures [1], were sometimes also treated by PC. According to current experience [27], radicular pain, epidural extension, and spinal cord compression were not considered as strict exclusion criteria; however, in these cases (n=8), PC was combined with steroids, surgery, or radiation therapy.

Table 1 Initial patient characteristics

Male/female	17/11 (61%/39%)
Median age	65 (40–89)
Median elapsed time from diagnosis to PC	66 months (0–132)
Stage I	3 (11%)
Stage II	4 (14%)
Stage III	21 (75%)
IgG	21 (75%)
IgA	5 (18%)
Light chains	2 (7%)
Previous treatments	
CT 1 line	10 (36%)
CT≥2 lines	15 (54%)
ASCT×1	3 (11%)
ASCT≥2	9 (32%)
Thalidomide	12 (43%)
Levels treated	
Dorsal vertebrae	57 (42[a])
Lumbar vertebrae	59 (33[a])
Sacrum	1
Others (pelvis)	1 (1[a])

CT Chemotherapy, *ASCT* autologous stem cell transplantation
[a] Number of fractures among the levels treated.

Percutaneous cementoplasty

PC procedures were performed under local anesthesia when a single vertebral level was treated (n=7) and under short general anesthesia when two or more levels were treated (n=27). A postero-lateral transpedicular approach was used for vertebral lesions, as previously described [20, 22]. One patient underwent extraspinal cementoplasty in the pelvis bone, using the approach reported by Kelekis et al. [19]. Before polymethylmethacrylate (PMMA, lopamidol, lopamiro 300; Bracco, Milan, Italy) injection, contrast venography was always performed to map the venous outlets and predict possible leakage pathways (Fig. 1). The needle was repositioned in cases where the risk of venous embolization was considered too high. PMMA opacified with barium sulfate was then injected under fluoroscopic guidance (biplanar fluoroscopic angiography suite, BV 3000; Philips Medical Systems, Best, The Netherlands), with careful observation for potential PMMA extra-osseous leaks. The mean volume of PMMA injected in each vertebra was 3.1 ml (range 1.5–7.5 ml), and a total of 8-ml PMMA was injected for the pelvic procedure. Finally, a post-cementoplasty CT scan was performed within 24 h to document any PMMA leakage. Post-cementoplasty thoracic X-rays or CT scan were performed in case of extra-osseous cement leakages detected by bone CT scan (n=8) or symptoms suggesting pulmonary embolization (n=2).

Clinical assessment and statistical analysis

The objective of this study was to investigate the potential effect of PC on pain and disability. Clinical outcome was assessed by one of us (NNTT) by comparing pre- and post-cementoplasty (day 30) pain scores, analgesic consumption, and performance status (PS). Pain score was assessed using a visual analogue scale (VAS) ranging from 0 (no pain) to 10 (maximal pain) [13]. Percentage of pain reduction was calculated using the following formula: Percentage of pain reduction=100×[(VAS before PC−VAS after PC)/VAS before PC]. PS was determined with the ECOG scale [29]. Statistical analysis was performed using a Student's t-test to compare pain scores. As the PS has only five levels, the assumption of a normal distribution is not possible, and we used the Mann–Whitney rank sum test, a nonparametric test, instead of the t-test, to assess difference in PS before and after PC.

Results

Patients

A total of 117 vertebrae, including 75 fractures, were treated by PC in 33 sessions (n=27 patients). In one additional

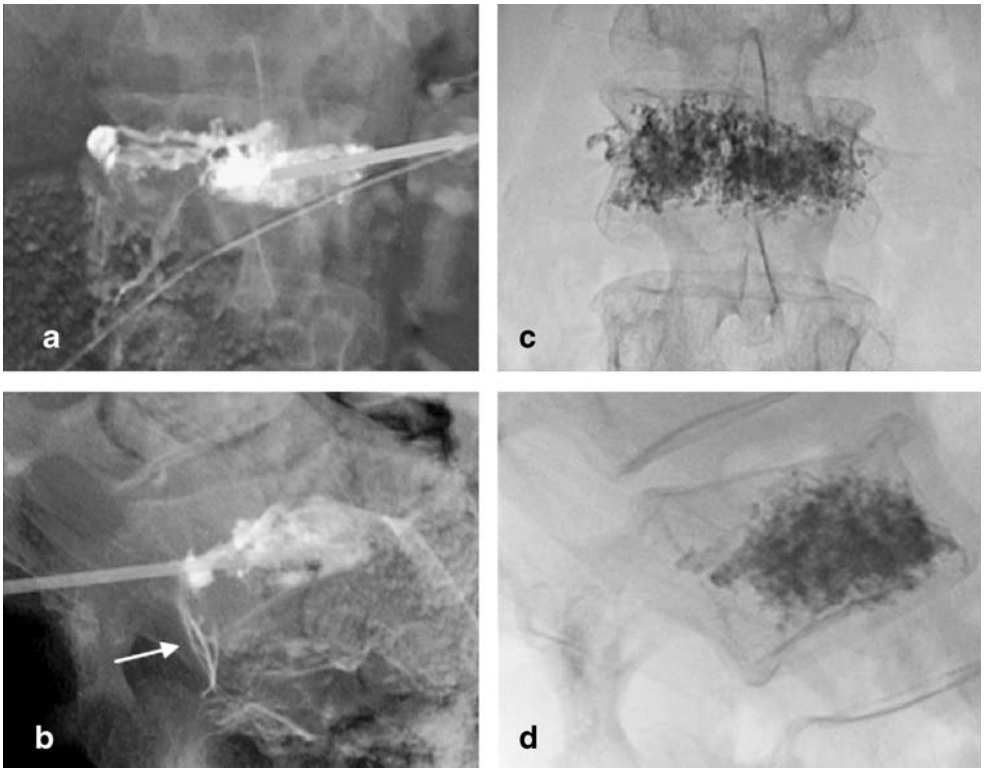

Fig. 1 Venography followed by vertebroplasty of a L3 compression fracture. **a** and **b** Antero-posterior and lateral views of the venography, respectively, with a small epidural leak (*arrow*). Venography here reflects classical vascular distribution as usually seen in MM. **c** and **d** Results of the vertebroplasty procedure, with adequate filling of the vertebral body, without leakage

patient, iliac and acetabular PMMA injections were performed for extensive pelvis involvement. Mean number of vertebrae that were treated in one session was 3.27, with a range from 1 to 9, and the different levels treated are shown in Table 1. Median follow-up after PC was 41 months (range 3–81), during which there was no clinical evidence of progressive disease at the sites of cement implantation. Five patients suffering from pain occurring later on at other sites received additional PCs. One of them had a total of three procedures over 5 months (Fig. 2).

Most patients required further therapies for MM progression, which always arose out of the sites previously treated by PC. At the time of data analysis, eight deaths had occurred, six from chemotherapy-related complications. The patient who underwent the pelvic procedure received a second autologous stem cell transplantation, followed by thalidomide and bortezomib treatments. She died from chemotherapy-related adverse events 2 years after the PC, but without progressive disease at the sites of cement implantation.

Safety and complications

The tolerance for the procedure was excellent for all patients. As assessed by control CT scan performed shortly after the intervention, eight cement leakages were documented (24%). They were, however, of small size (<1 cm) and clinically not relevant. A single cement leakage along the L5 nerve root was correlated with the appearance of a transient sensitive defect in this territory, which resolved within 3 weeks. Two patients had transient thoracic pain or dyspnea after PC, but pulmonary embolization was excluded in both cases by lung CT scan and pulmonary scintigraphy.

Efficacy

To determine efficacy of the procedure, three parameters were analyzed at day 30: pain control through VAS scores, decrease in opiate analgesics consumption, and ambulation/autonomy through PS scale. According to current experience, day 30 represents a valuable time point to assess the stability of PC efficiency [25]. At that time, outcome data were available for 30/34 procedures, four patients being lost for follow-up.

Pain control

Mean VAS fell down from 7.48 (range 4–10) before PC to 2.1 (range 0–10) after PC ($p<0.001$). This represents a 70–100% pain reduction for 21 procedures (70%), a 50–69% pain reduction for 4 PC procedures (13.3%), and a low response (0–49% of pain relief) after 5 procedures (16.7%).

Opiate analgesic consumption

Consumption of opiate analgesics was reported for every patient before and after PC, with three patients who did not take any opiate or derivatives before the procedure. Opiate consumption could be interrupted after 16/27 procedures (59.3%) and partially reduced after 6/27 (22.2%). Only five

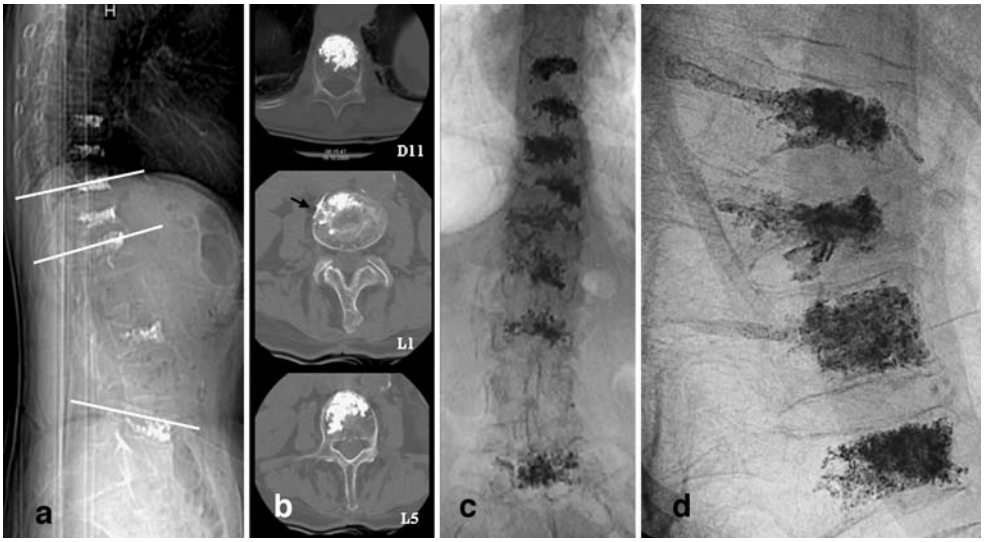

Fig. 2 Vertebroplasty at multiple levels (76-year-old patient). Lateral (**a**) and axial (**b**) CT scan views: result of PC in one step at seven levels (D9 to L1, L3, L5) in this patient with debilitating dorso-lumbar pain secondary to multiple compression fractures. A small PMMA leakage is observed on the axial view of L1 (*arrow*). **c** Two months later, the patient presented with a painful fracture of L2, which was located between two previously treated vertebrae. Panoramic view of the total eight levels treated. **d** Two months later, pain recurred secondary to a D7 compression fracture. D6 and D8, which showed vertebral body and pedicular infiltration, were also treated by PC. Lateral view after D6–D9 PC. Outcome was excellent, with only minimal pain and full autonomy for more than 3 years

patients had to maintain their preoperative level of opiates. Overall, we noted a mean decrease in opiate dose of 70.4%.

Performance status

Most patients had major ambulation problems related to pain secondary to fractures and bone infiltration, interfering with their daily occupations and impairing their autonomy. Mean PS improved from 1.9 to 0.86 after PC (p=0.001). Variations of the number of patients for each PS score before and after PC are shown in Fig. 3. No patient experienced worsening of ambulatory capacities.

Discussion

This retrospective analysis of heavily pretreated (median time from diagnosis to PC: 66 months) MM patients showed that PC may induce a rapid and sustained decrease in pain related to tumor bone infiltration and, consequently,

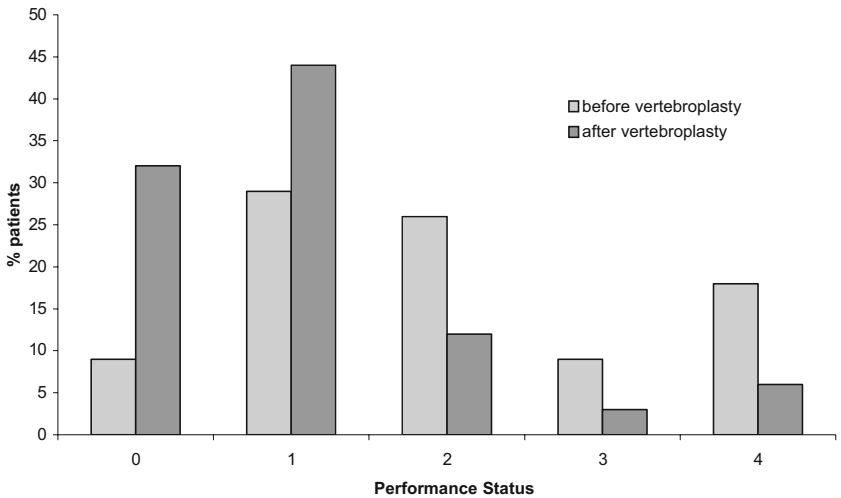

Fig. 3 Performance status scores before and after PC. The proportion of patients in each level of PS—according to the ECOG scale—is shown before and after PC. *0* Fully active, able to carry on all pre-disease performance without restriction. *1* Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. *2* Ambulatory and capable of all selfcare but unable to carry out any work activities, up and about more than 50% of waking hours. *3* Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours. *4* Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair

Table 2 Reports of percutaneous cementoplasty in multiple myeloma patients

	Procedure	Nb of patients	Median age	Nb of levels treated	% Levels fractured	% Cement leakage	Outcome: pain relief	Outcome: functional amelioration	Complications
Cotten et al. [3]	Vertebroplasty	8	59.5	10	NA	60	Mild to marked pain relief in all patients	NA	None
Dudeney et al. [6]	Kyphoplasty	18	63.5	55	100	4	Improvement in pain	Improvement in function	None
Diamond et al. [5]	Vertebroplasty	7	68	14	100	0	75% Improvement in pain scores	50–60% Improvement in functional status	None
Bartolozzi et al. [2]	Percutaneous vertebroplasty and kyphoplasty	14	54	19 (10 vertebroplasties and 9 kyphoplasties)	100	NA	Improvement in VAS (9/10 to 3/10)	amelioration in Karnofsky (50 to 70)	None
Ramos et al. [24]	Percutaneous vertebroplasty	12	66	19	100	84	Improvement in VAS (7.5/10 to 3.7/10)	Improvement in ECOG (3.1 to 2.5)	None
Present study	Percutaneous cementoplasty	28	65	119	63	24	Improvement in VAS (7.48/10 to 2.1/10)	Improvement in ECOG (1.9 to 0.86)	1 Transient sensory loss

a major reduction in opiate analgesic consumption. The benefit provided by PC is also revealed by the overall improvement in ambulatory capacities and daily occupational abilities of the patients, as shown by the better ECOG scale after the procedure. Despite inclusion of severely compromised patients, no major adverse effect was observed, with a single case of transient L5 sensitive defect secondary to cement leakage. Overall, these observations suggest that PC is an attractive new therapeutic approach for improving the quality of life of MM patients.

Our data confirm and extend those recently reported in a few studies exploring the PC or kyphoplasty in MM (summarized in Table 2). In these studies, the number of treated patients was limited, the procedure was usually performed on a single or a small number of vertebrae, and mainly, compression fractures were considered for PC or kyphoplasty. In this paper, we show in a larger series of patients that PC can be applied to several levels within the same procedure, with a median of three vertebrae treated in a single step (range 1–9). Our data also suggest a benefit from PC even in the absence of MM-induced bone fracture. For MM patients with a long history and diffuse bone involvement, restricting PC to the more symptomatic vertebrae or compression fracture could be deleterious in view of the well-known risk of fracture in involved vertebrae neighboring a cemented level [1, 24]. Extending PC to non-broken vertebrae (37% in our series) might considerably improve the antalgic effect obtained by the procedure. Indeed, pain relief by PC at one defined level might sometimes uncover pain in surrounding vertebrae, and we actually observed that the pain killing effect was less complete when a single vertebra was treated. Therefore, in the particular case of MM, we propose to consider PC not only for compression fractures but also for adjacent vertebrae involved with the tumoral process.

With a median follow-up of 41 months after PC, we did not see any evidence of progression at the site of PC, while all patients relapsed eventually or even died from MM. This clinical observation supports the hypothesis of an anti-tumor effect mediated by hyperthermia arising during PMMA polymerization, as suggested by extended tumor necrosis observed in and around PMMA [26].

Due to the simultaneous advances in transplantation strategies and in innovative therapies, MM patients experience longer survival, underlining the importance of quality of life issues. Whether PC has to be considered as a first-line option for symptom management—in conjunction with other standard therapies—or as a saving option

for long-lasting bone pain refractory to established therapies remains to be better defined. This should be the issue of large-scale prospective studies in the future.

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